Figure 1

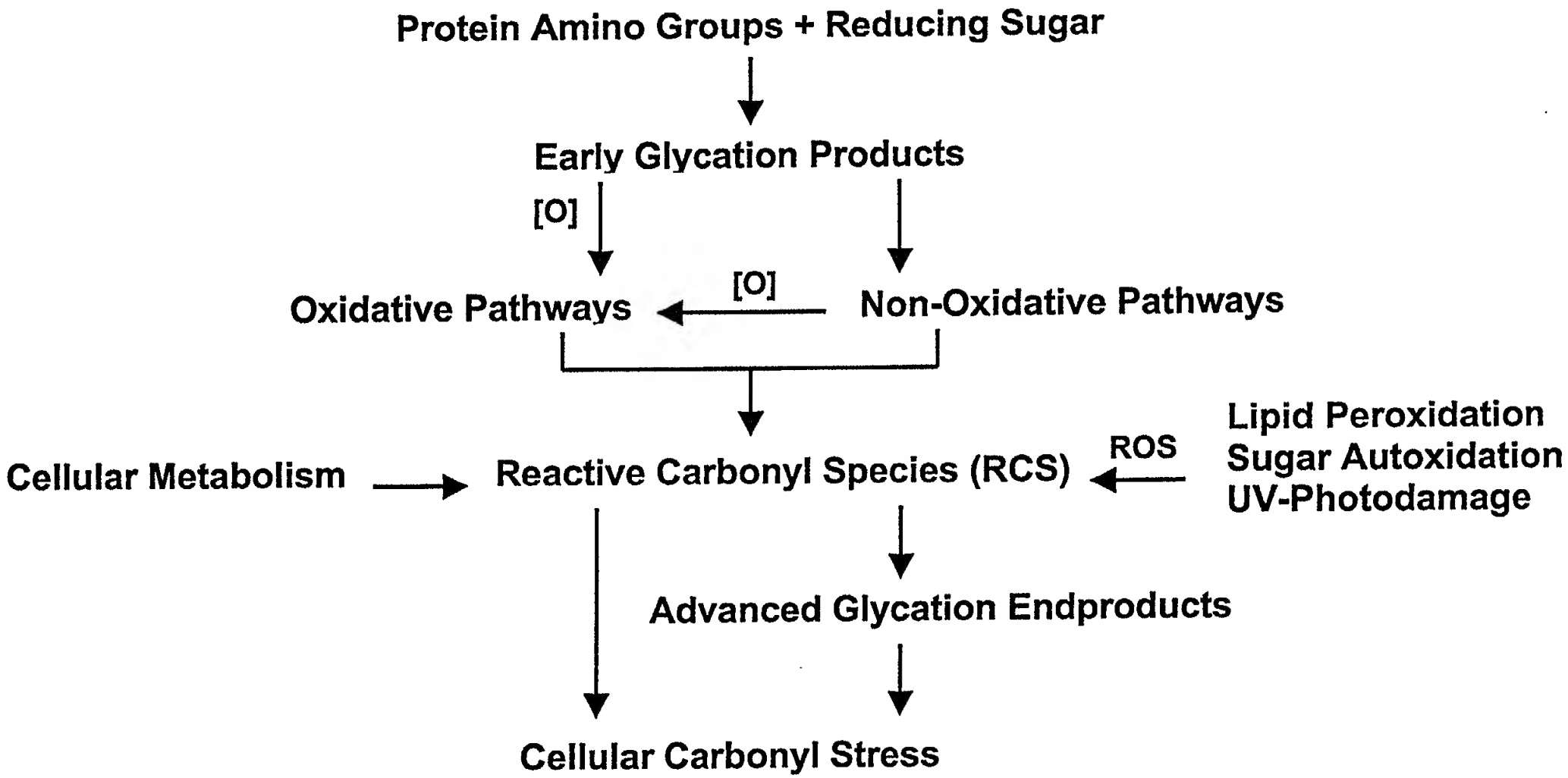
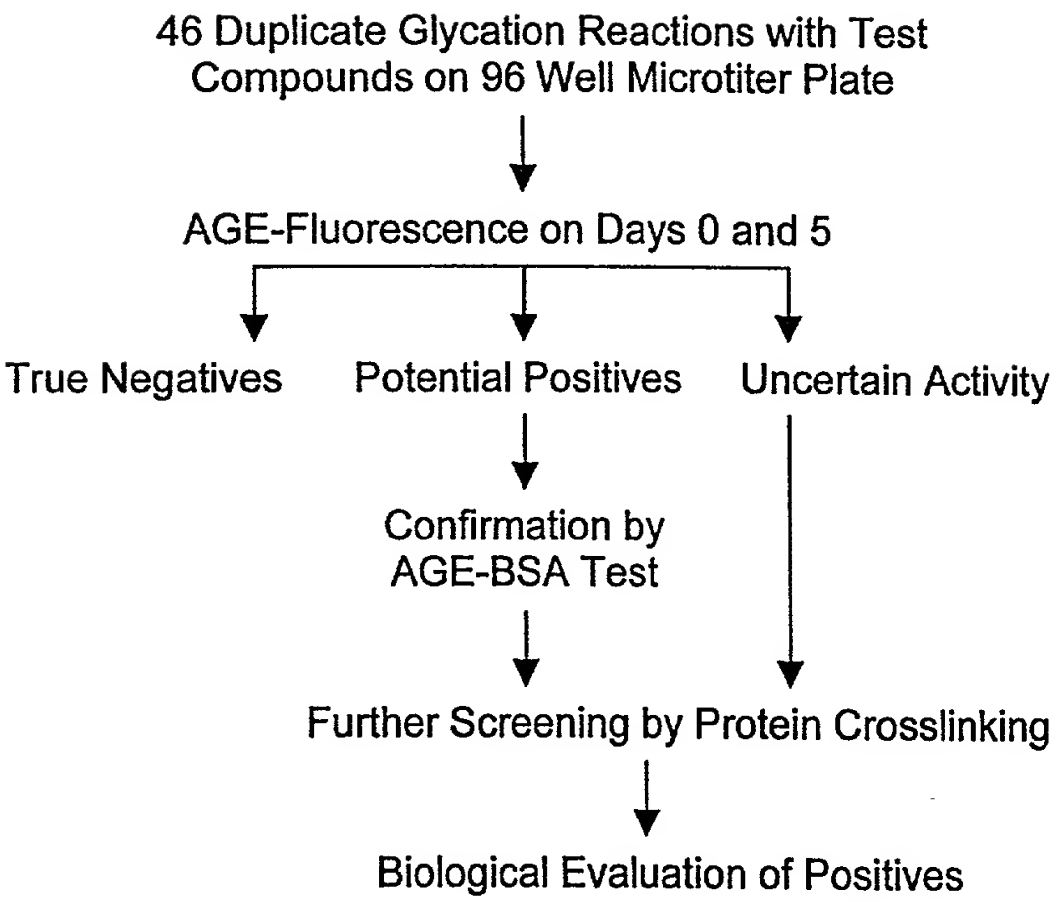
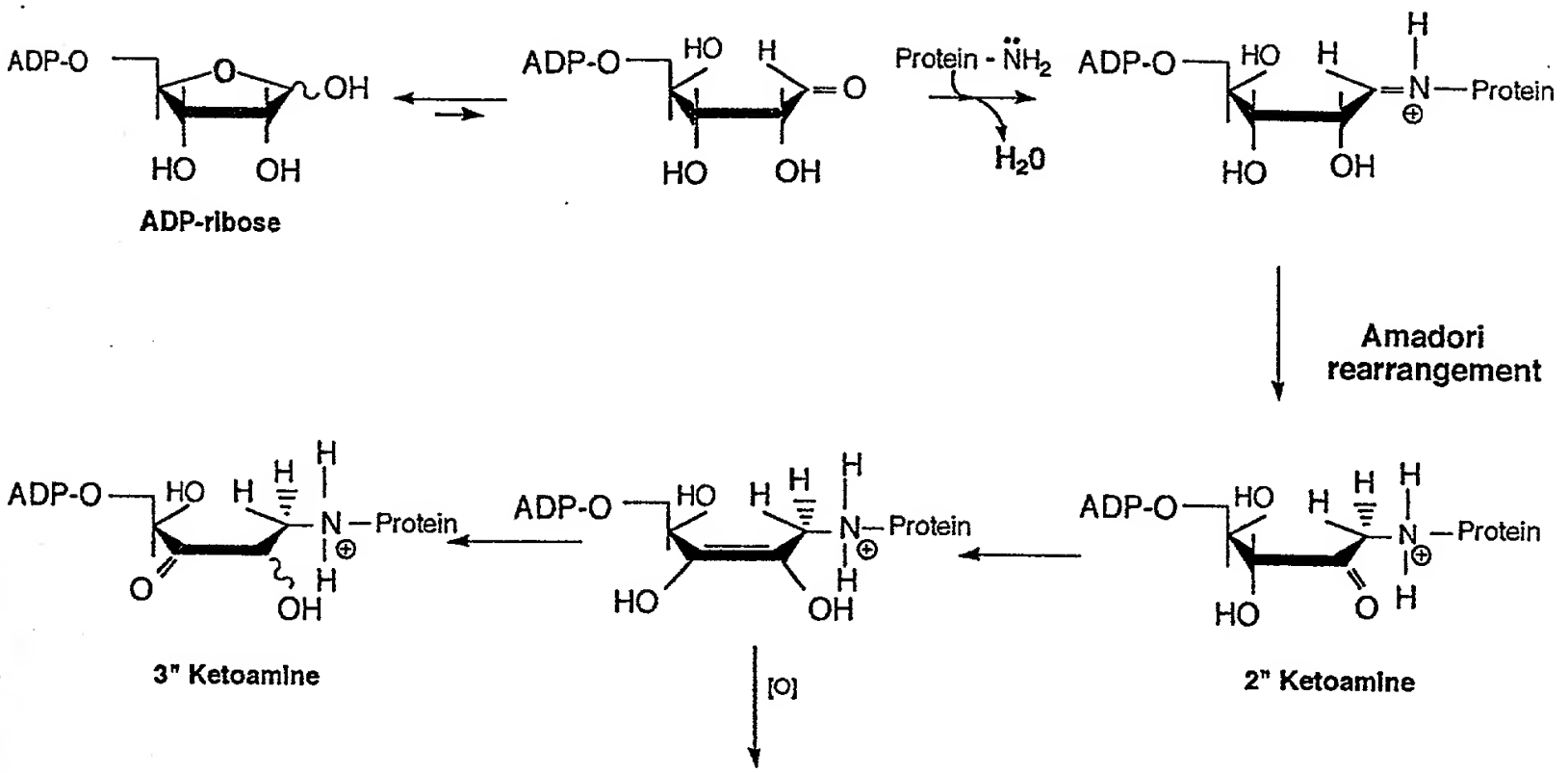


Figure 2


46 Duplicate Glycation Reactions with Test Compounds on 96 Well Microtiter Plate
AGE-Fluorescence on Days 0 and 5
True Negatives
Potential Positives
Uncertain Activity
Confirmation by AGE-BSA Test
Further Screening by Protein Crosslinking
Biological Evaluation of Positives



Protein Advanced Glycation End Products (AGEs)
[N^{ε}-(carboxymethyl)lysine, pentosidine, protein cross-links]

Figure 3

AGE-Inhibitor Screening: Time course of AGE-fluorescence

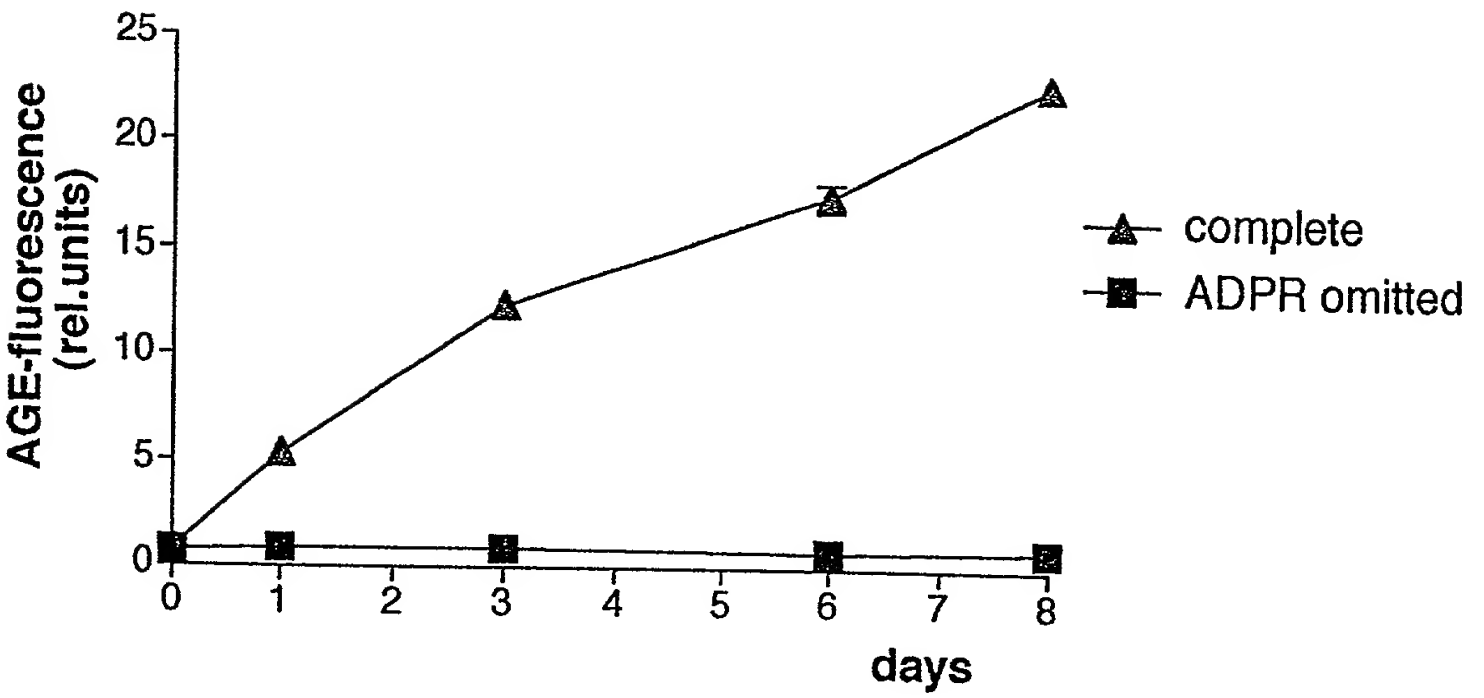


Figure 4

Fluorescence yield of various sugars and histone H1 over 7 days

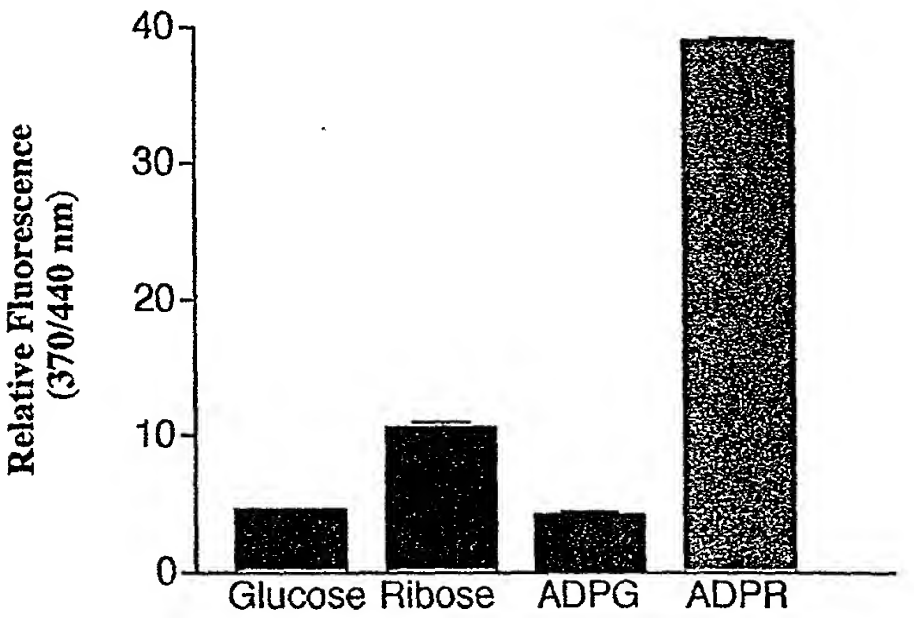


Figure 5

Effectiveness of histone H1 as a target protein for glycation

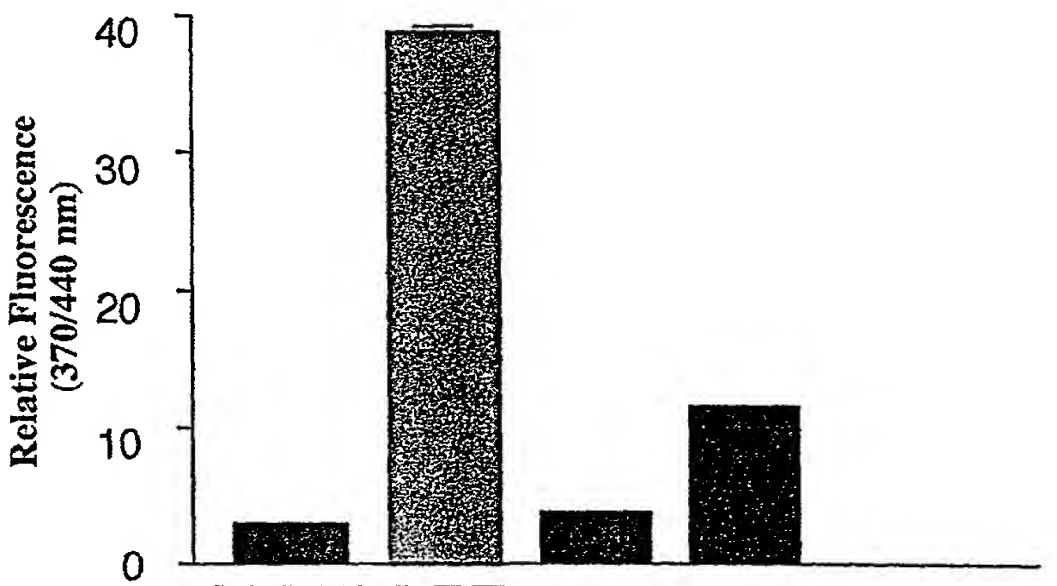


Figure 6

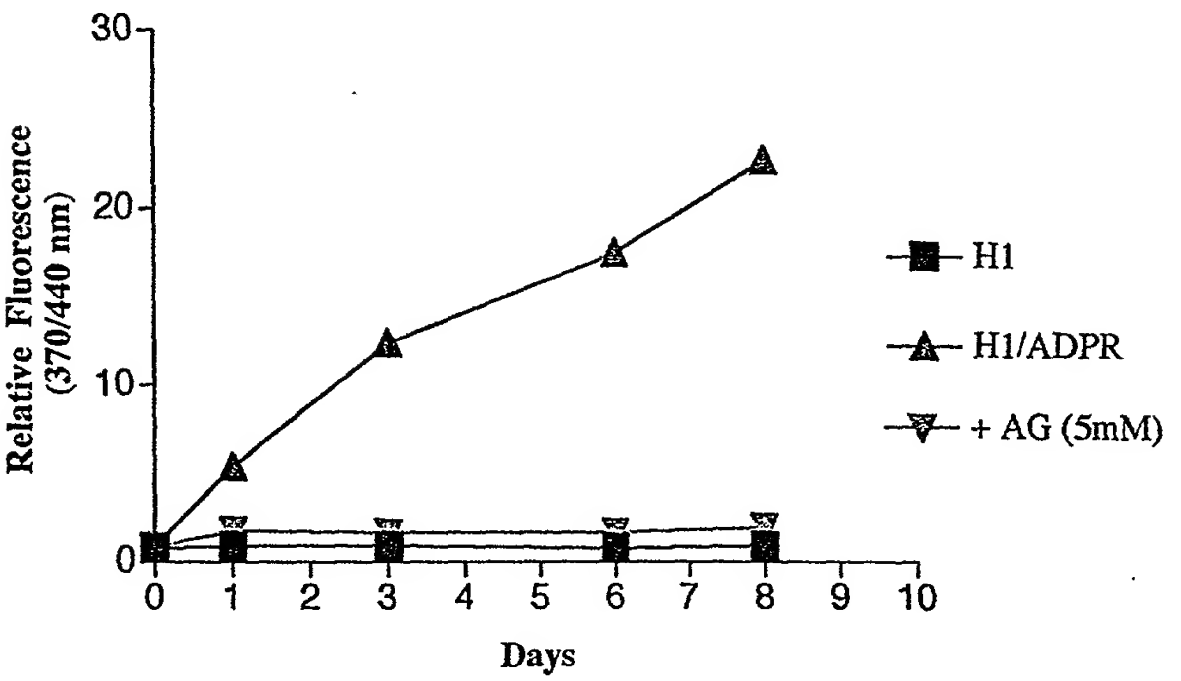

Aminoguanidine inhibits glycation of histone H1 by ADP-ribose
Relative Fluorescence (370/440 nm)
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10
Days
H1
H1/ADPR
+ AG (5mM)

Figure 7

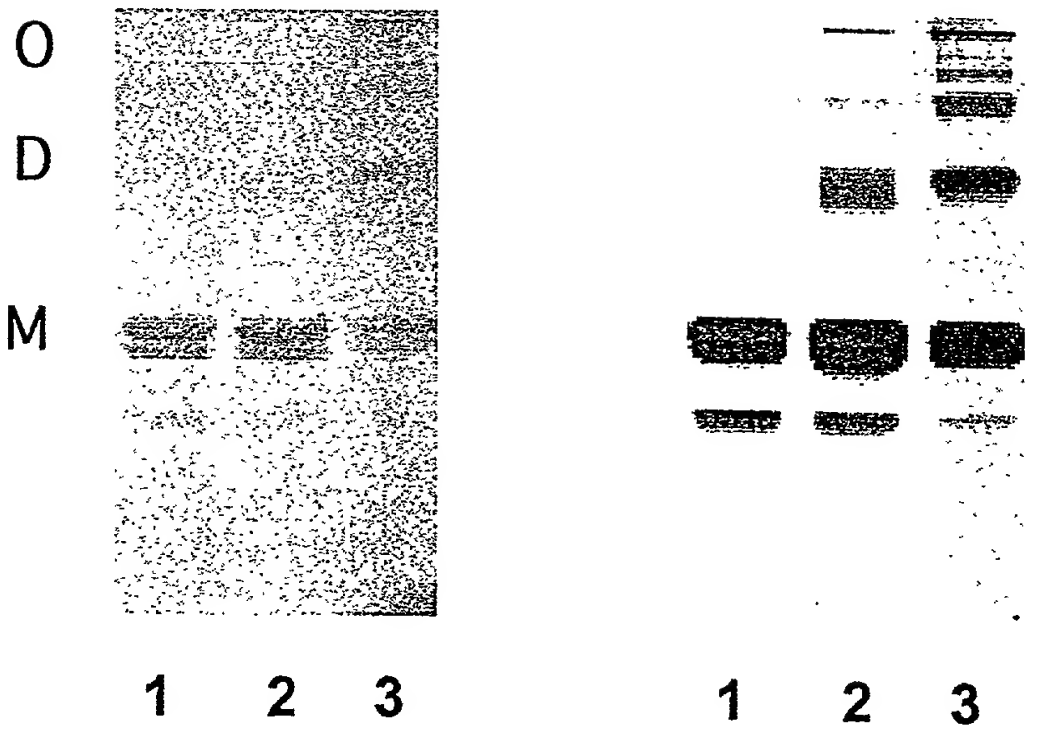


Figure 8

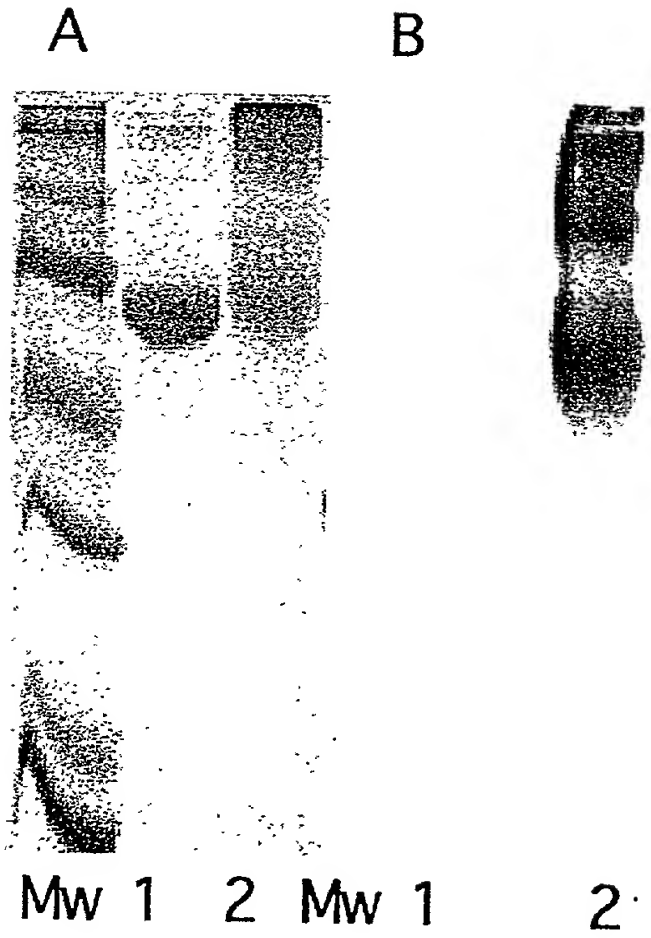


Figure 9

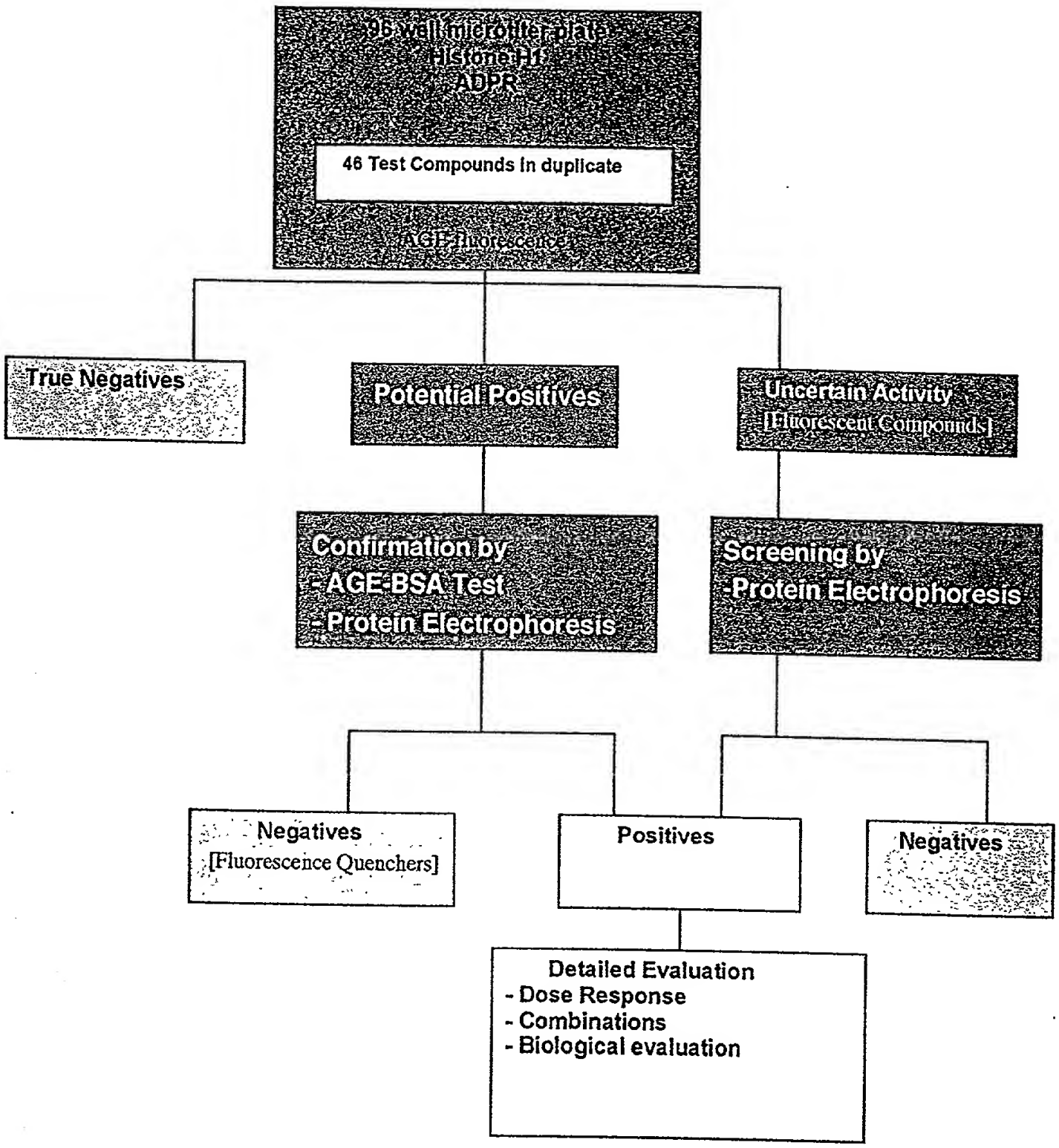

96 well microtiter plate
Histone H1
ADPR
46 Test Compounds in duplicate
AGE-Fluorescence
True Negatives
Potential Positives
Uncertain Activity
[Fluorescent Compounds]
Confirmation by
- AGE-BSA Test
- Protein Electrophoresis
Screening by
-Protein Electrophoresis
Negatives
[Fluorescence Quenchers]
Positives
Negatives
Detailed Evaluation
- Dose Response
- Combinations
- Biological evaluation

Figure 10

AGE-Inhibitor Screening
Example: L-cysteine

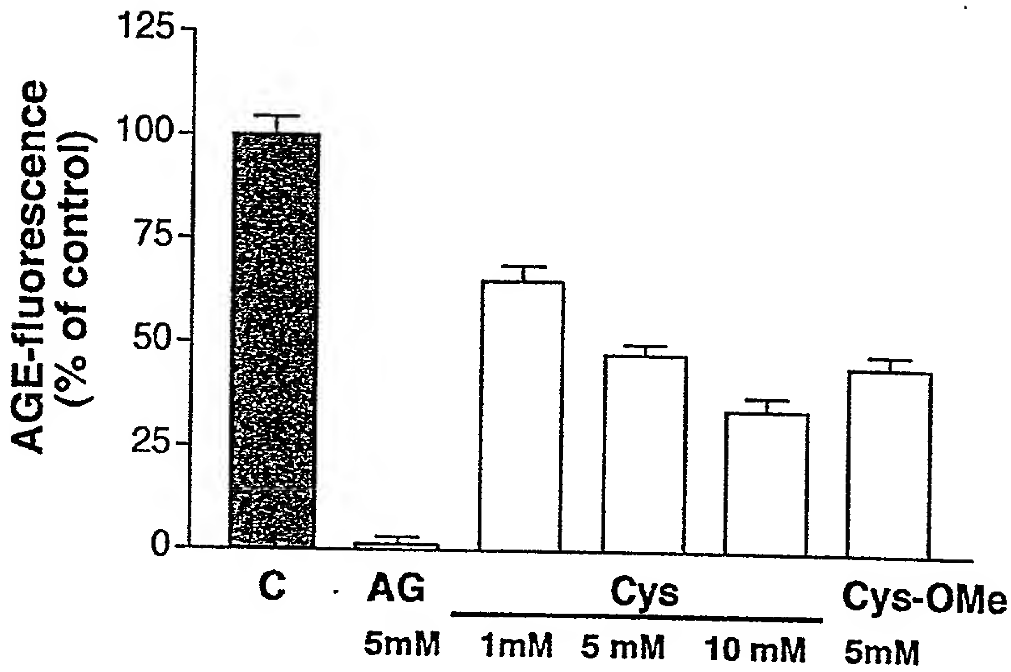


Figure 11

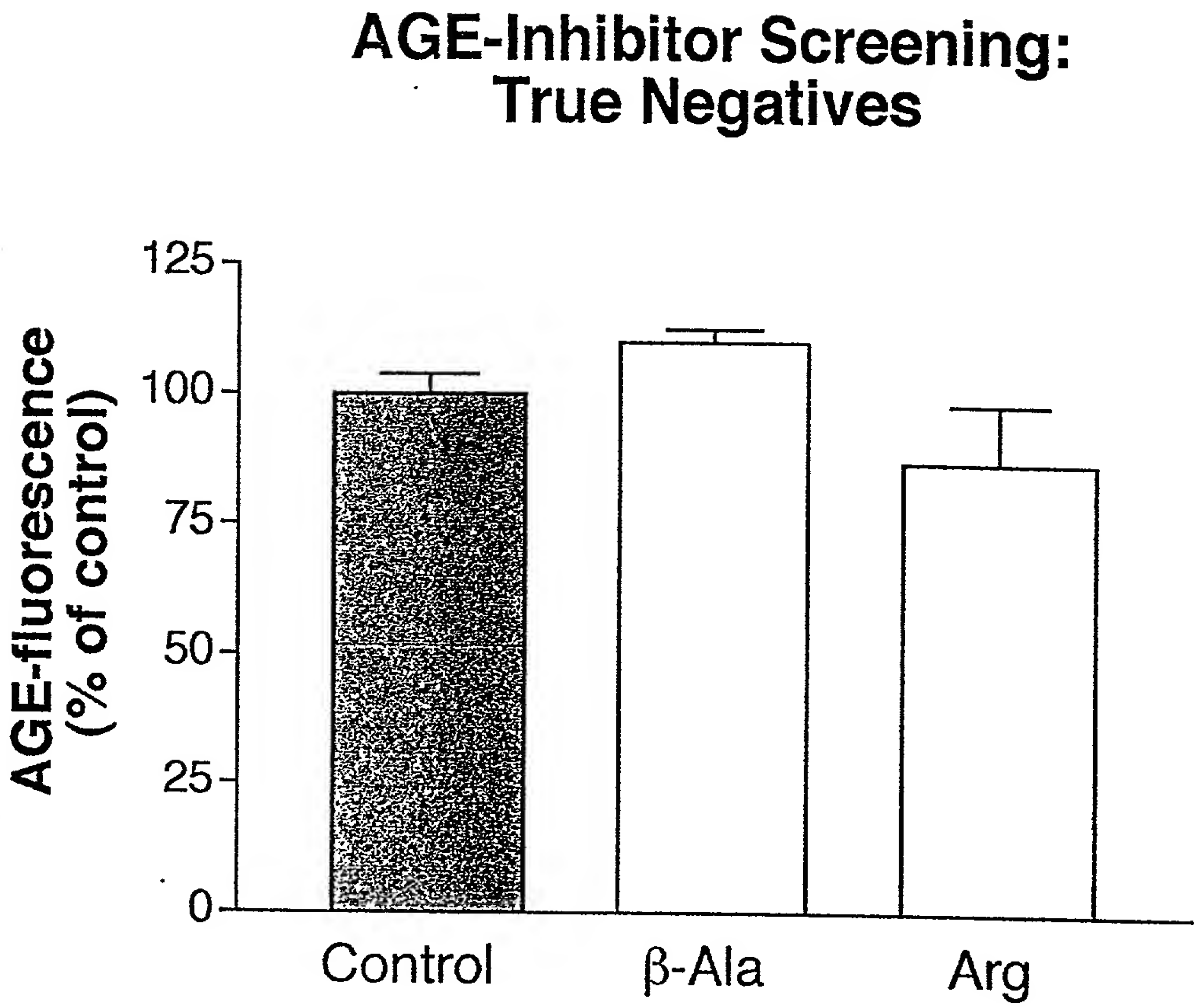

AGE-Inhibitor Screening:
True Negatives
AGE-fluorescence
(% of control)
125
100
75
50
25
0
Control
β-Ala
Arg

Figure 12

Confirming Potential Positives I: the AGE-BSA Test

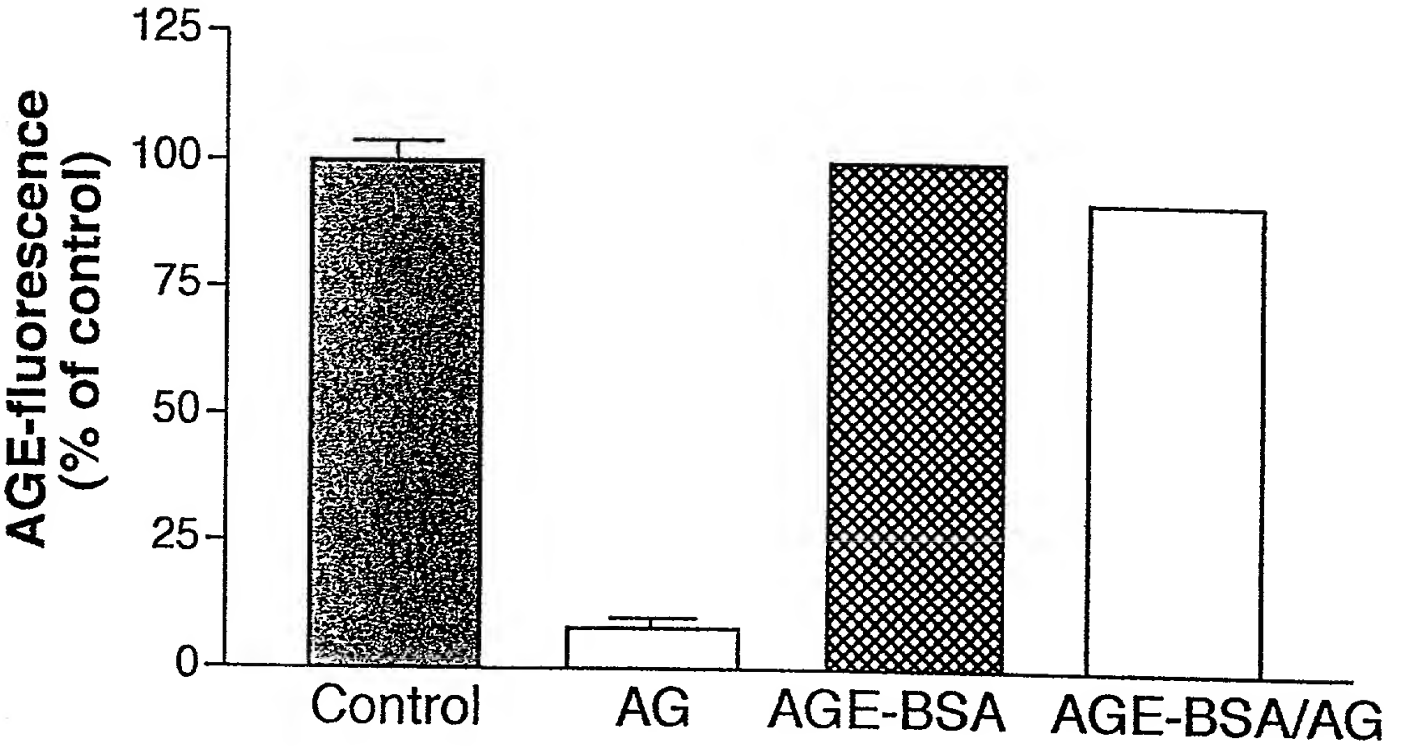


Figure 13

Confirming Potential Positives II: Protein Electrophoresis

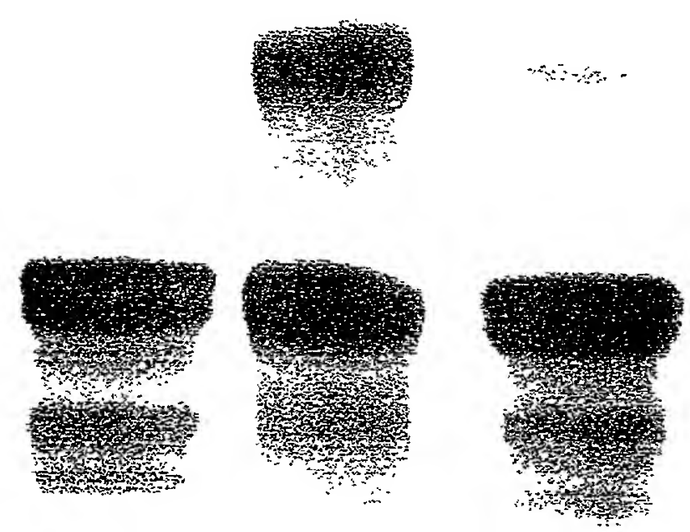


Figure 14

Figure 15

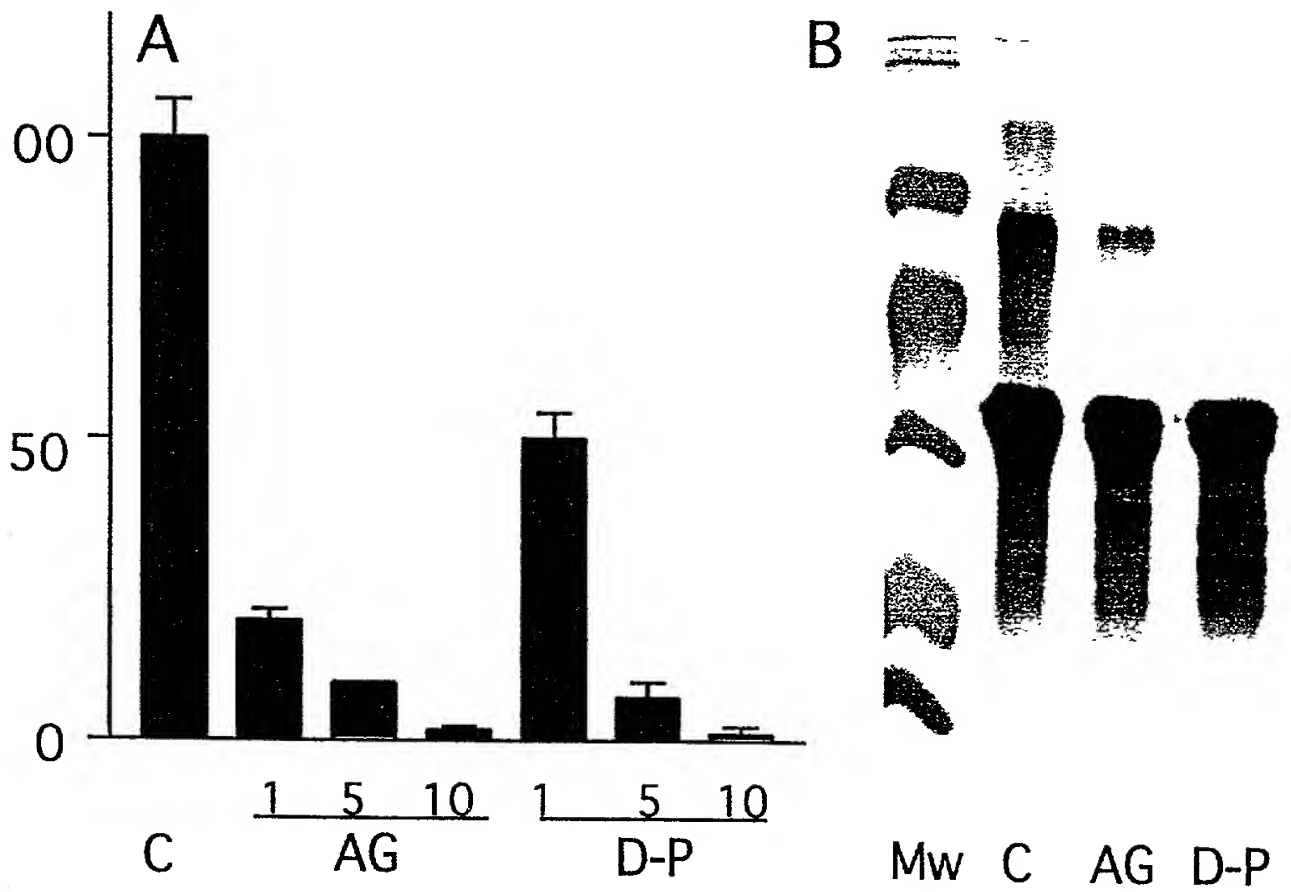
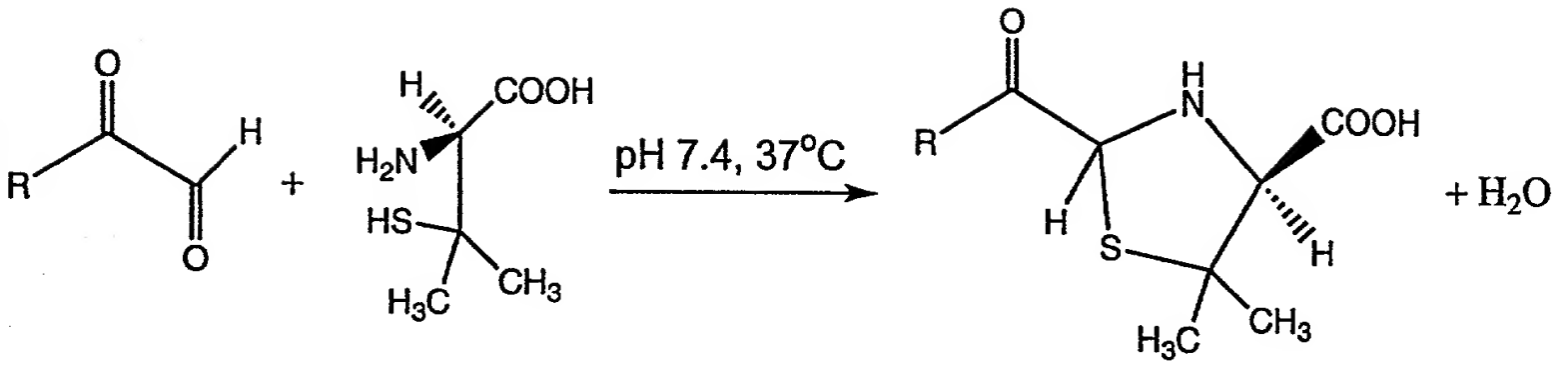
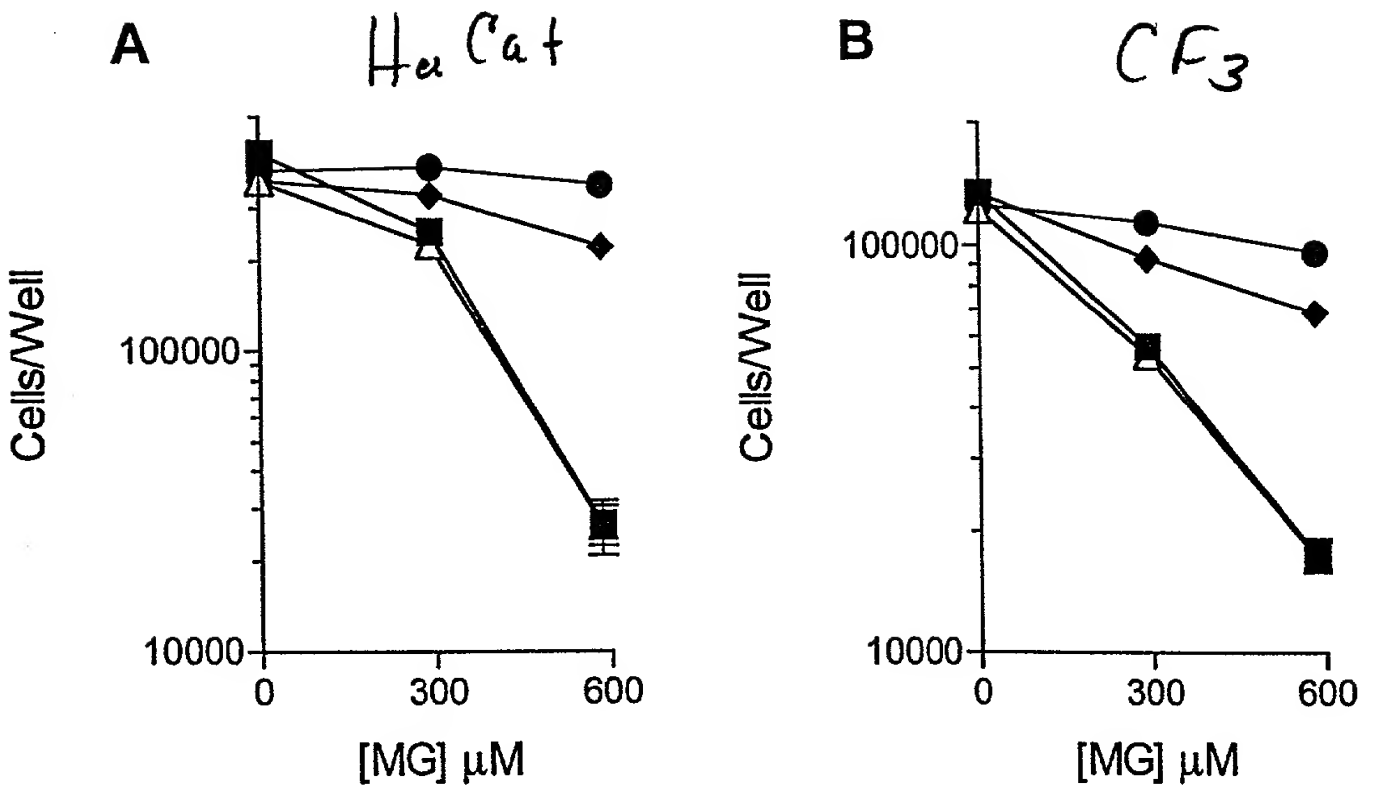

A
AGE-fluorescence
(% of control)
100
50
0
1 5 10 1 5 10
C
AG
D-P
B
D
M
Mw C AG D-P

Figure 16



R = CH_3 or C_6H_5

Figure 17

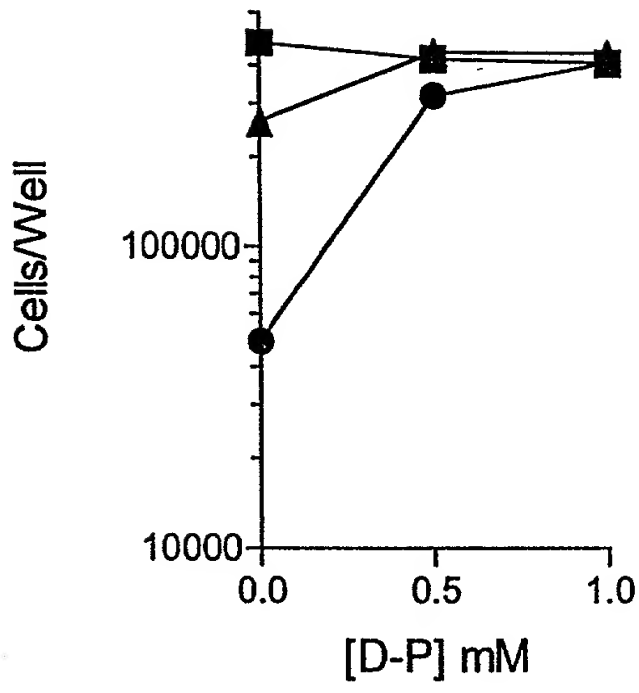


■ : α-dicarbonyl alone
△ = L alanine (1mM)
◆ = aminoguanidine
● = D-penicillamine

Figure 18

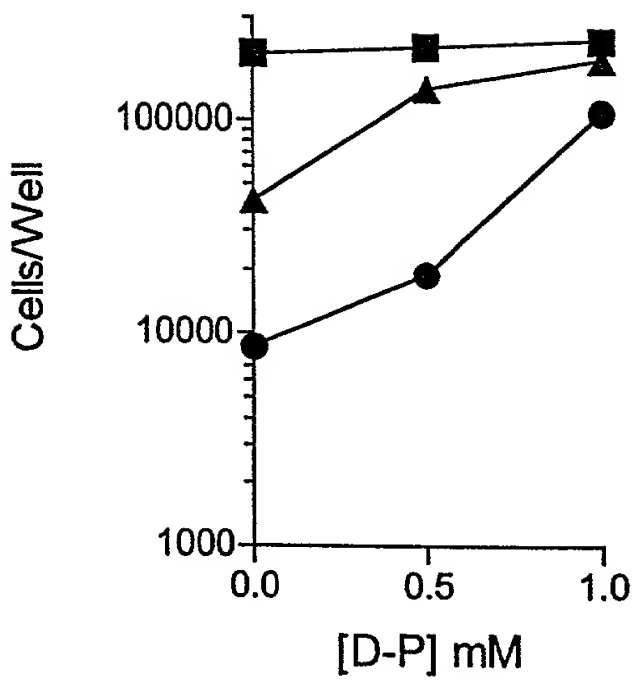
HaCaT

A



CF_3

B



■ : no methylglyoxal
▲ : methylglyoxal (300μM)
● : methylglyoxal (600μM)

D-P : D-penicillamine

Figure 19